Analytical profile of Lisdexamfetamine dimesylate (Vyvanse™)

Valerie Kamb
Johnson County Crime Lab
Mission, KS 66202
Valerie.Kamb@jocogov.org

Submitted: 14 March 2008
Accepted: 9 April 2008

Introduction

Vyvanse™ (lisdexamfetamine dimesylate) is a drug in a new class of long-acting prodrug stimulants for Attention-Deficit/Hyperactivity Disorder (ADHD) (Fig. 1). Vyvanse™ was approved by the FDA in February 2007 and is a Federal Schedule II controlled substance. Vyvanse™ is manufactured by New River Pharmaceuticals, Inc. and distributed by Shire, Inc.

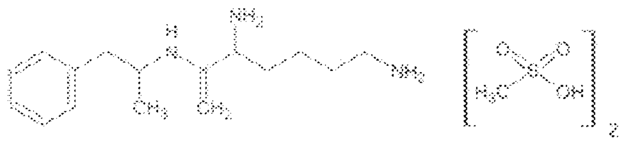

Fig. 1 Lisdexamfetamine dimesylate: MW = 455.60

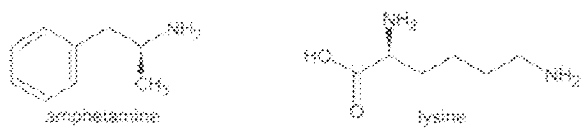

Fig. 2 Amphetamine and lysine structures

Lisdexamfetamine (aka "Lisdex" or "LDX") is unique from other ADHD drugs because it is a prodrug of *d*-amphetamine designed in part to reduce the potential for abuse. A prodrug is a pharmacological substance which is therapeutically inactive until metabolized in the body. In the case of Vyvanse™, *d*-amphetamine is covalently linked to the amino acid *l*-lysine (Fig. 2). Once lisdexamfetamine passes through the gastrointestinal tract and liver, it is converted to active *d*-amphetamine [1].

Vyvanse™ is currently supplied in three dosage strengths with the following capsule colors and logo markings:

Dosage	Capsule Colors	Imprint
30 mg	white/orange	NRP104 30 mg
50 mg	white/blue	NRP104 50 mg
70 mg	blue/orange	NRP104 70 mg

During the second quarter of 2008, three more dosage strengths (20, 40 and 60 mg) will become available for use [2].

Experimental (Reference Standard Data)

Reference standard: A 200 mg (white) reference powder was obtained from Shire, Inc., and ten 30 mg capsules were purchased from a local pharmacy.

GC-MS analysis: A portion of the reference powder was dissolved in methanol. Analysis was performed on a HP 6890/5973 GC-MS (EI) with a HP-35 ms column using a ramped general temperature program.

FTIR analysis: FTIR analysis was performed using a Perkin Elmer Spectrum 100 with a single bounce diamond ATR.

Alkaline hydrolysis procedure: One capsule was tested with alkaline hydrolysis to determine if amphetamine could be produced *in vitro*. The contents were made basic with saturated NaOH and heated in a 70° C water bath for approximately 30 minutes. The sample was then extracted with $CHCl_3$ and analyzed by GC-MS.

Results and Discussion

Four color tests were performed on both the capsule and reference powder with the following results:

Marquis	orange → brown
Liebermann's	orange
sodium nitroprusside	no color change
acidified cobalt thiocyanate	no color change

The mass spectrum (Fig. 3) of the methanol extract for lisdexamfetamine produced a base ion of m/z 84 with a molecular ion of m/z 263. Other major ions present include m/z 191, 91, 172, and 155.

FTIR-ATR data (Fig. 4) produced principle absorption bands at 1668, 1545, 1513, 1187, and 1036 cm^{-1}.

The alkaline hydrolysis of lisdexamfetamine produced a trace of amphetamine (Figs. 5 and 6).

Conclusion

Analytical data consisting of color tests, GC-MS and FTIR-ATR was presented to aid the analyst with the identification and confirmation of lisdexamfetamine. The alkaline hydrolysis procedure has shown that amphetamine can be cleaved from the lysine group although an appreciable amount was not produced under the stated conditions.

Acknowledgements

1. Sandra Williams, Shire, Inc. for providing the standard
2. Agent Tim McKibben, CBI, for sharing his data

References

1. Vyvanse™ Medication Guide", Shire Pharmaceuticals Inc., retrieved from http://www.vyvanse.com on September 11, 2007.
2. Press release announcement retrieved from http://www.threadbiotreatments.com on March 3, 2008.

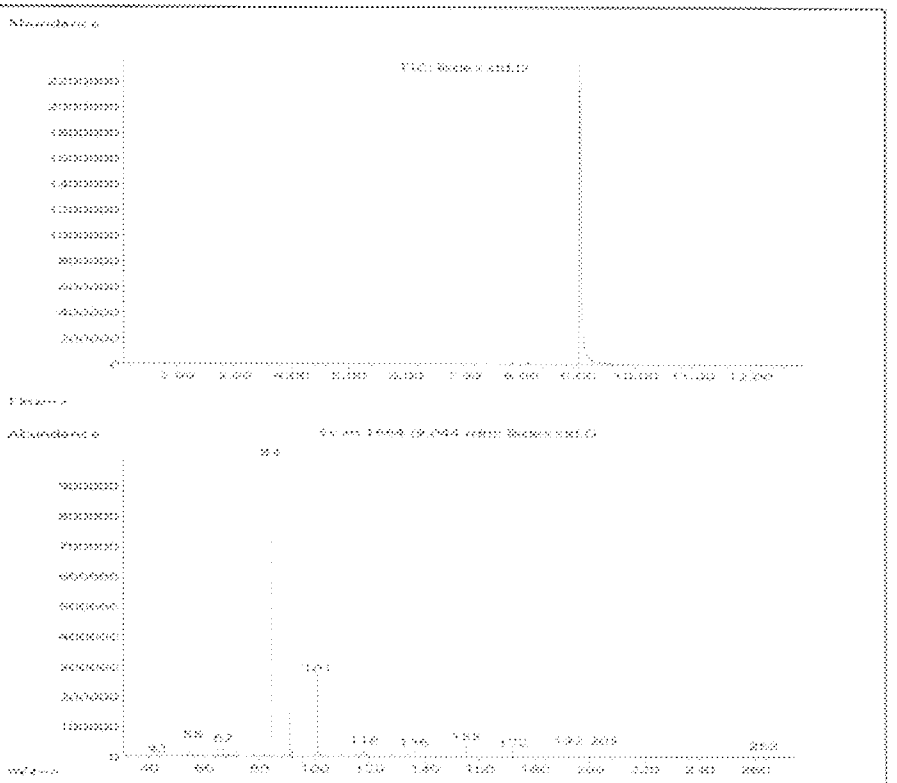

Fig. 3 TIC and mass spectrum of Isaxamfetamine; MW – 263.14

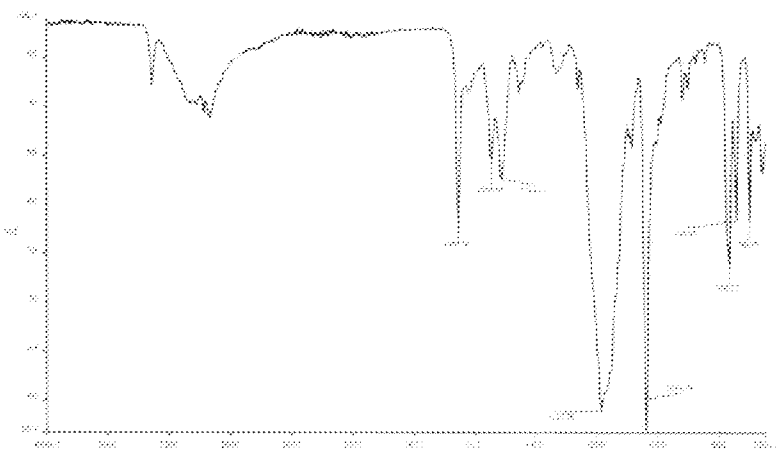

Fig. 4 FTIR-ATR of isaxamfetamine dimesylate

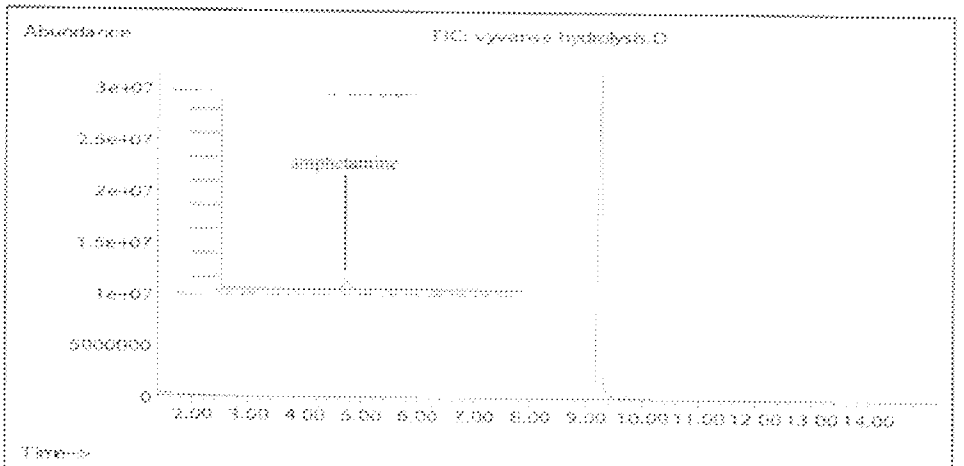

Fig. 5 TIC of amphetamine peak after alkaline hydrolysis of lisdexamfetamine

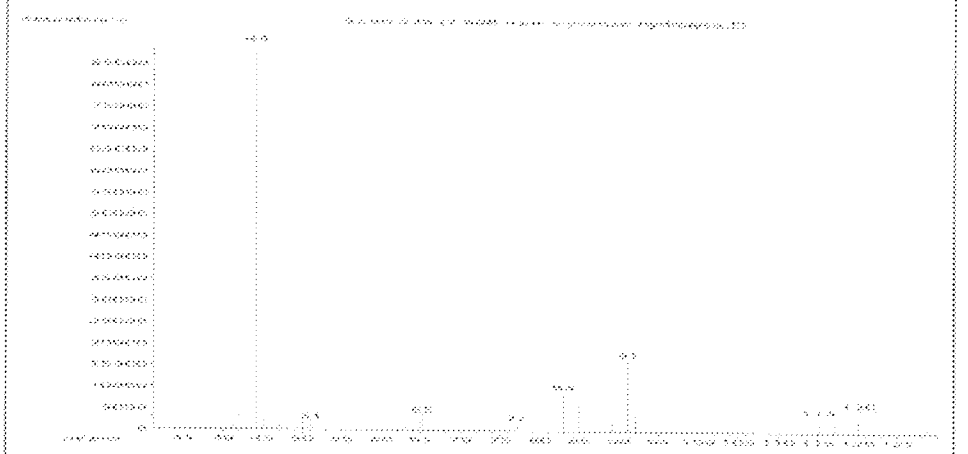

Fig. 6 Mass spectrum of amphetamine peak